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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/648,270	05/15/1996	YITZHAK TOR	A-63463-1	8895

7590 09/13/2004

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EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 09/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/648,270	TOR ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07/27/2004 (status inquiry)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant is advised that the Notice of Appeal dated April 26, 2001 is vacated and that prosecution is reopened. Because the following includes new grounds of rejection, this is a non-final Office action.

The Abstract of the Disclosure is objected to because is does not meet the requirement of the MPEP for US application. Correction is required. See MPEP §608.01(b).

Applicant is reminded of the proper content of an Abstract of the Disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains.

If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure.

If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement.

In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof.

If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following: (1) if a machine or apparatus, its organization and operation; (2) if an article, its method of making; (3) if a chemical compound, its identity and use; (4) if a mixture, its ingredients; (5) if a process, the steps. Extensive mechanical and design details of apparatus should not be given.

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts, compounds or compositions, the general nature of the compound or composition should be given as well as its use, e.g., "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary. Complete revision of the content of the abstract is required on a separate sheet.

Claims **1-43** have been cancelled, no claims have been amended, the disclosure has not bee amended, and no new claims have been added as of the mailing date of this Office action. A declaration by Professor Thomas Meade has been received and is addressed in the following Office action. No additional Information Disclosure Statements (IDSs) have been received as of the date of this Office action. The PTO-892 attached hereto notes three additional US patent references previously supplied in incomplete form by applicant.

Claims **44-49** remain in the case.

Claims **44-49** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims **44-49** are broadly descriptive of the claimed invention. However, the specific embodiments are limited to a very small number of examples directed exclusively to how to make certain substituted phenanthrolines and metal complexes thereof. Examiner notes that none of the specific examples includes a description of how to make phenanthrolines or transition metal complexes thereof with linkages to the base moiety of:
i) a nucleoside,
ii) a nucleotide,
iii) a phosphoramiditylated nucleoside ("a phosphoramidite nucleotidyl moiety"),
iv) an oligonucleotide ("a nucleic acid moiety"), or
v) an oligonucleotide analogue ("a nucleic acid analog"). Examiner has also again reviewed all of the submitted prior art and finds no teaching which overcomes the lack of disclosure of how to make the claimed compounds, OR any showing that compounds of the type claimed are

stable, a serious question in view of the phosphatase activity of certain metal complexes and transition metal complexes well known in the art as enzymes (see PTO-892 reference **SA** (**Lehninger**) at page 185, Table 8-2). Examiner notes in particular the subject matter of claims **46-49** wherein a transition metal complex is linked to a nucleotide with one ribophosphate ester linkage or an oligonucleotide substituent with multiple ribophosphate diester linkages and a well known capability to self associate (hybridization). Therefore, while it is true that applicant has pictured compounds which read on the instant claims with chemical formulas numbered "9" to "12" in the disclosure at pages 12-13 and expressed an intent to make same at page 3, lines 24-26, applicant has failed to provide the minimum necessary instructions to the ordinary practitioner required to actually make one or more of the structures shown, or proof that applicant actually isolated and characterized any one of the structures shown as of the instant filing date. As noted in *Brenner v. Manson,* 148 USPQ 689 (S. Ct., 1966) at p. 696, column 1, "[A] patent is not a hunting license. It is not a reward for the search, but compensation for its successful completion (emphasis added)."

Applicant's arguments with respect to claims **44-49** have been considered but are deemed to be moot in view of the new grounds of rejection. The following is a response to the declaration of record filed under 37 C.F.R. §1.131.

Examiner has reviewed the extensive CV, the supplied reference (cited herein as PTO-892 ref. **Y**), and the declaration of Professor Thomas H. Meade. Prof. Meade argues that one of ordinary skill, making reference to cited prior art references all now of record, may make the compounds claimed herein without difficulty. Examiner respectfully disagrees, firstly because the compounds made in reference **Y** are structurally different from the instant claimed compounds (complex attached to sugar moiety, not the base moiety). Examiner disagrees secondly because the syntheses of the non-phosphorylated compounds in reference **Y** do not support the extrapolation of the instant disclosed phenantholine syntheses to compounds containing one or more phosphite or phosphate ester linkages because said linkages are potentially subject to spontaneous cleavage in the presence of a neighboring transition metal complex as noted in the rejection supra.

Thirdly, examiner respectfully disagrees because the standard is not a theoretical one limited only by imagination, but rather a practical one. The standard for patentability is whether, "as of the filing date has applicant actually made examples which read on the instant

claims?" and has applicant characterized the products of these labors in sufficient detail to establish that the products are real and provide one of ordinary skill with sufficient information to confirm that a repetition of the disclosed processes of making produce the compounds as claimed. Examiner refers Prof. Meade to the history of the well respected book series known as Organic Syntheses wherein procedures for making various organic compounds initially were not published until the process has been successfully reproduced in the chemical synthesis laboratory of another practitioner, a key step in the early establishment of integrity in the science of organic synthesis.

Granted, organic synthesis of complex molecules including lengthy nucleic acid sequences has become routine courtesy of modern spectroscopic (NMRs, Mass Spec., etc.) and chromatographic (HPLC, etc.) methodologies. But this is not the issue here. Applicant's, in analogy with the standards originally propounded by the editors of Organic Syntheses, need to show that what they have imagined has been reduced to practice and how this reduction to practice was accomplished. Without such a disclosure requirement, the deal offered by the USPTO becomes little more than an invitation to withhold subject matter and receive a patent, which is in effect permitting either
i) the patenting of a Trade Secret (compounds can be made but the process remains secret), or
ii) patenting of compounds which could not be made in which case the public's trust in the patent system is compromised because the ordinary practitioner will be unable to reproduce the patent's disclosed methods of making because the organic syntheses (processes) imagined could not, or can not, be made to work.

The deal offered to all applicants by the USPTO is that, in return for disclosure by applicant of how to make and/or use the claimed invention, the USPTO grants the right to exclude another from using the claimed and enabled subject matter (invention) for a period of years. The payoff to the public for the limited grant of this right is that the technology disclosed and enabled may, after the right to exclude has expired, may be used by the public without limit thereby expanding the public technology knowledge base. However in the present case, should a patent be granted, following the patent expiration the public will end up with an empty bag, because this applicant has failed to complete the disclosure requirement which is the prerequisite to the bargain, which bargain is the legal basis for the grant of what is known as a U. S. Patent.

Claims **44-49** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention; the scope is excessive in view of the disclosed exemplifications.

The definitions of substituents in claims **44-49** is/are directed to a vast number of chemical compounds which have not been described in the instant disclosure in a manner permitting the ordinary practitioner to have the guidance necessary to make any of the compounds encompassed. Examiner finds no such compounds disclosed in the "Examples" section.

Applicant's arguments with respect to claims **44-49** have been considered but are deemed to be moot in view of the new grounds of rejection.

Claims **44-49** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims includes phenanthrolines or transition metal complexes thereof with linkages to the base moiety of:
i) a nucleoside,
ii) a nucleotide,
iii) a phosphoramiditylated nucleoside ("a phosphoramidite nucleotidyl moiety"),
iv) an oligonucleotide ("a nucleic acid moiety"), or
v) an oligonucleotide analogue ("a nucleic acid analog"). Said breadth is unsupported by any examples wherein any species with all of the noted structural elements has been disclosed as having been made anywhere within the disclosure.

B. The nature of the invention is limited to chemical compounds as noted in the previous section.

C. The state of the prior art is well described by the art presently of record and does not include any reference or combination of references usable to establish anticipation or obviousness.

D. The level of one or ordinary skill is extensive but does not extend to making compounds containing transition metal complexes and either a phosphate ester or ribophosphodiester linkages.

E. The level of predictability in the art is low because the art fails to provide any exemplifications wherein nucleotides or oligonucleotides are stable to phosphate ester hydrolysis when a transition metal complex is present in the same molecule.

F. The amount of direction provided by the inventor is limited to statements of intent to make the compounds of the invention.

G. The existence of working examples is limited to three examples wherein phenanthrolines and metal complexes thereof are prepared. However, there are no examples wherein the phenanthroline or metal complex thereof has been attached to a nucleoside, a nucleotide or an oligonucleotide.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because of a complete lack of examples showing that the compounds claimed can be synthesized, how such syntheses are conducted, and the conditions under which the compounds wherein phenanthroline complexes and nucleotide or oligonucleotide moieties are both present are in fact isolable and stable.

Claims **46 and 47** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims **46 and 47** the term "nucleic acid moiety" as defined in claim **47** to "comprise[s] [a] nucleic acid analog" is technically incorrect because the former is properly a substituent and the latter is a compound.

Applicant's arguments with respect to claims **46 and 47** have been considered but are deemed to be moot in view of the new grounds of rejection.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(f) or (g) prior art under 35 U.S.C. §103(a).

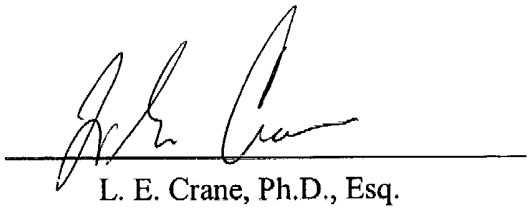
Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 703-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
08/27/2004



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